PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference I30265PCT	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/EP2005/000873	International filing date *(day/month/year)* 28.01.2005	Priority date *(day/month/year)* 28.01.2004
International Patent Classification (IPC) or national classification and IPC INV. G01N33/68		
Applicant IMMATICS BIOTECHNOLOGIES GMBHet al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 9 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in Item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in celectronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
25.07.2005	08.08.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Lüdemann, S Telephone No. +49 89 2399-7842

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2005/000873

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

   ☐ international search (under Rules 12.3 and 23.1(b))
   ☐ publication of the international application (under Rule 12.4)
   ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-21 as originally filed

   Sequence listings part of the description, Pages

   1-11 as originally filed

   Claims, Numbers

   1-40 as originally filed

   Drawings, Sheets

   1/4-4/4 as originally filed

   ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 18, 37-38, 19-36, 39, 40

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 18, 37-38, 19-36, 39, 40

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees, the applicant has:
   - ☐ restricted the claims.
   - ☐ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☐ neither restricted nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
   - ☐ complied with.
   - ☒ not complied with for the following reasons:

     see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
   - ☐ all parts.
   - ☒ the parts relating to claims Nos. Invention 1: claims 1-17 .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	-
	No:	Claims	1-17
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1-17
Industrial applicability (IA)	Yes:	Claims	1-17
	No:	Claims	-

2. Citations and explanations (Rule 70.7):

   see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment on

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

Re Item III.

1. As has been indicated by the International Searching Authority, claims 18, 37 and 38 lack clarity (Art. 5 and 6 PCT) to such an extent that a meaningful complete search could not be performed.

2. According to R. 66.1(e) PCT, claims, in respect of which no ISR has been established need not be the subject of International Preliminary Examination.

Re Item IV.

The separate inventions/groups of inventions are:

Invention 1: claims 1-18, 37, 38
A method for identifying and quantifying tumour-associated peptides, comprising the steps: providing a first sample of tissue or cells, providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample, obtaining peptides from the first and the second sample, separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples, mixing of the so modified peptides from both samples, determining the amino acid sequences of the peptides, and determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics.

Inventions 2: claims 19-36, 39, 40 (all partially)
The tumour-associated peptide having the amino acid sequence according to seq. id. no. 1, its use, pharmaceutical compositions and methods based on it, nucleic acids, vectors encoding it and cells transfored by the latter.

Inventions 3-37: claims 19-36, 39, 40
The tumour-associated peptides having the amino acid sequence according to seq. id. no. 2-36 their use, pharmaceutical compositions and methods based on them, nucleic acids, vectors encoding them and cells transfored by the latter.

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

Claims 1 and 19 lack unity a priori, since they do not share any common technical features, besides that they are both related to tumour-associated peptides. Claim 1 is related to a method for identifying and quantifying tumour-associated peptides, comprising the steps: providing a first sample of tissue or cells, providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample, obtaining peptides from the first and the second sample, separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples, mixing of the so modified peptides from both samples, determining the amino acid sequences of the peptides, and determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics.
Claim 19 is related to a tumour-associated peptide having an amino acid sequence that is selected from the group consisting of SEQ ID-No. 1 to 36 from the accompanying sequence protocol, wherein said peptide has the ability to bind to a molecule of the human major histocompatibility complex (MHC) class-1.
Said claims also solve different problems. The problem to be solved by claim 1 is to be seen as provision of a method for identifying and quantifying tumour-associated peptides, while the problem to be solved by claim 19 is the provision of specific peptides with specified sequences having the ability to bind to a molecule of the MHC class-I.
Furthermore, also claim 19 lacks unity of invention, since neither the functional feature "having the ability to bind to a molecule of the MHC class-I" can be seen as the common inventive concept linking the different embodiments of claim 19 (see abstract and introduction of D4 cited in the ISR) nor do the different sequences claimed under claim 19 share a common structural feature which would define the contribution made to the prior art. Thus, also the subject-matter of claim 19 is not so linked as to form a single general inventive concept.
In conclusion, neither the technical features in common to the groups of claims nor the problem solved by each of the different group of claims provide a corresponding special technical feature, which establishes a single general inventive concept linking any of the sets of claims. Thus, the technical relationship between the subject-matter of the sets of claims is missing and the requirement for unity of invention referred to in R. 13.1 PCT is

not fulfilled.

Re Item V.

1. Reference is made to the following documents:

   D1: WO 03/025576 A (XZILLION GMBH & CO. KG; THOMPSON, ANDREW, HUGIN; HAMON, CHRISTIAN; SCH) 27 March 2003 (2003-03-27)

   D2: MARTIN DANIEL B ET AL: "Quantitative proteomic analysis of proteins released by neoplastic prostate epithelium." CANCER RESEARCH, vol. 64, no. 1, 1 January 2004 (2004-01-01), pages 347-355, XP002359082 ISSN: 0008-5472

   D3: MORITZ BERND ET AL: "Approaches for the quantification of protein concentration ratios." PROTEOMICS, vol. 3, no. 11, November 2003 (2003-11), pages 2208-2220, XP002359083 ISSN: 1615-9853

   D4: WEINSCHENK T ET AL: "Integrated functional genomics approach for the design of patient-individual antitumor vaccines" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 62, no. 20, 15 October 2002 (2002-10-15), pages 5818-5827, XP002266492 ISSN: 0008-5472

   D5: BEARDSLEY RICHARD L ET AL: "Optimization of guanidination procedures for MALDI mass mapping." ANALYTICAL CHEMISTRY. 15 APR 2002, vol. 74, no. 8, 15 April 2002 (2002-04-15), pages 1884-1890, XP002359084 ISSN: 0003-2700

   D6: LEMMEL CLAUDIA ET AL: "Differential quantitative analysis of MHC ligands by mass spectrometry using stable isotope labeling" NATURE BIOTECHNOLOGY, vol. 22, no. 4, April 2004 (2004-04), pages 450-454, XP002359085 ISSN: 1087-0156

2. Novelty and inventive step

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-3 is not new in the sense of Article 33(2) PCT.

2.2 Document D1 discloses (the references in parentheses applying to this document): A method for identifying and quantifying tumour-associated peptides, comprising the steps (see claims 25-26 and p. 45-46):
(I) providing a first sample of tissue or cells (p. 45 and 46),
(ii) providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample (p. 45 and 46),
(iii) obtaining peptides from the first and the second sample (p. 45 and 46),
(iv) separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples (claim 6),
(v) mixing of the so modified peptides from both samples (p. 45 and 46 and Example 3b),
(vi) determining the amino acid sequences of the peptides, and determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics (p. 45 and 46 and Example 3b).

2.3 Document D2 discloses (the references in parentheses applying to this document): The preamble is anticiapted by the title and abstract. Steps (i)- (iii) (corresponding to steps a)-c) of claim 3) are anticipated by the abstract, p. 348, Materials and Methods, left col., second paragraph. Step (iv) (corresponding to steps d) -g) of claim 3) are anticipated by p. 348, Materials and Methods, left col., 4th paragraph to right col., first paragraph. Steps (v) and (steps h-i of claim 3) are anticipated by p. 348, Materials and Methods, right col.,second paragraph and fig. 3 and tables 1-3.

2.4 Accordingly, document D3, which is a review on approaches for the quantification of protein concentration ratios discloses the subject-matter of claims 1-3 in chapter 3, in particular chapter 3.2.

2.5 Dependent claims 4-17 do not appear to contain any additional features which, in combination with the features of any of the claim to which they refer, meet the requirements of the PCT with respect ot novelty or inventive step.